Docket No.: 511582001621
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Daniel E. AFAR et al.

Application No.: 10/010,667

Filed: December 6, 2001

For: PEPTIDES DERIVED FROM STEAP-1

Art Unit: 1642

Examiner: Gary B. Nickol, Ph. D.

TOPICS FOR INTERVIEW

Applicants appreciate the willingness of the Office to conduct an interview on this case concerning STEAP-1. The sole outstanding rejection is formally made under 35 U.S.C. § 112; however, the real basis appears to be a lack of utility under 35 U.S.C. § 101.

The claims are directed to peptides that represent portions of the STEAP-1 protein that are able to raise antibodies which are immunoreactive with the STEAP-1 protein. The Office has not questioned this ability, nor has the Office has questioned that the specification teaches how to make and use the antibodies raised. For example, page 20, lines 29-30, specifically state that STEAP antibodies are useful in prostate cancer therapeutic strategies, diagnostic and prognostic assays. Page 21 is a reminder that methods to prepare antibodies are well known in the art and some discussion of what these art-known ways are, is set forth there. Page 22 sets forth three of the four peptides set forth in claim 40 as being particularly useful and the fourth peptide is exemplified in a

working example. Known ways to humanize antibodies, etc. are also referred to. As set forth on page 27, STEAP-1 protein is expressed at high levels in several human cancers, including prostate, bladder, colon and ovarian and Ewing carcinoma. As noted, STEAP-1 protein in normal tissue is largely restricted to the prostate. Page 28, lines 18-20, state that since STEAP-1 is uniformly expressed at high levels over the surface of prostate glandular epithelia, immunotherapeutic intervention strategies that target extracellular STEAP epitopes are possible. Cancer immunotherapy using anti-STEAP antibodies is specifically set forth on page 29, lines 23-31, where it is clearly stated that methods of conducting such therapy are known in the art. The referred-to sections are merely exemplary of the guidance provided in the specification that the antibodies raised with respect to the claimed peptides are useful both for diagnosis and therapy of specified tumors.

Applicants believe that the Office does not question that the application is enabling with respect to teaching how to execute these uses of the invention, provided that the underlining natural behavior of STEAP-1 protein is such that application of these art-known methods with the novel antibodies raised using the claimed peptides provides a useful result. In order for that result to occur, the Office argues that applicants must:

1. demonstrate the absence of the STEAP-1 protein in normal tissue as compared to cancer tissue; or

2. demonstrate that STEAP-1 protein is present in patient cancer samples from tissues where STEAP-1 is normally absent.

With respect to the first item, it may be correct that the high levels of STEAP-1 in normal prostate make it difficult to utilize STEAP-1 protein levels as a marker for prostate cancer.

However, the presence of STEAP-1 protein in normal prostate does not preclude the use of STEAP-1 antibodies for the immunotherapeutic treatment of prostate cancer. While normal prostate tissue is as vulnerable as the cancer tissue, perhaps, to treatment by these antibodies, this is of no consequence as the prostate is a disposable organ. There is nothing of record which would indicate that it is incredible to treat a cancer with antibodies to a tumor-associated antigen and the well-known examples of Herceptin® and Rituxan® are proof that this is the case.

Further, although the *levels* of protein in prostate may not be diagnostic of prostate cancer, clearly the histochemical patterns exhibited using the STEAP-1 antibody to map the distribution of STEAP-1 protein clearly distinguishes normal prostate from, for example, prostate carcinoma. This is clearly shown in Figure 8 of the application. In addition, since other normal tissue does not produce STEAP-1 protein, detection of STEAP-1 protein in these tissues is evidence of metastasis in patients with prostate cancer.

In summary, even though STEAP-1 protein is produced in normal prostate, this does not preclude the use anti-STEAP-1 antibodies to treat prostate cancer; indeed, the high levels of STEAP-1 in the prostate may actually be helpful to mediate effective treatment. Further, by using histoimmunochemical methods, cancerous prostate can be distinguished from normal. And it may not even be necessary to test particular prostate cancers for the presence of STEAP-1, since as shown in Figure 5 and Figure 6, all samples of prostate cancer tested express this protein.

The Office acknowledges that normal tissues other than prostate have essentially undetectable levels of STEAP-1 protein, but asserts that it is not sufficient to demonstrate that various cell lines derived from pancreatic, colon, bladder, EWS, breast, testicular, cervical, and ovarian cancer, as well as ALL, show high expression levels for this protein. The Office argues that

as this has been shown only in cancer cell lines, this is insufficient proof that the protein will be present in actual cancer samples. In support, the Office quotes generalized statements that petri-dish cancer is poor representation of malignancy. The Office states that although protein may be produced by a cancer cell line, the corresponding human cancer may not produce this protein. The argument is based on the concept that the culture environment is different from the environment *in vivo*.

No doubt this is true, but that does not mean that it follows that a protein expressed in cancer cell lines would not be expressed in the corresponding cancer or that the expression of the protein in the relevant cell line is meaningless. There is no evidence of record showing that proteins highly expressed in a cancer cell line were not expressed in the cancer from which it was derived. In addition, absolute certainty is not required. A utility need only be specific, substantive, and credible. The production of STEAP-1 protein by the multiplicity of cell lines shown in Figures 5 and 6 would clearly indicate to the skilled artisan that it is highly probable that this protein is expressed in at least some cancers of the corresponding organ. And, since these organs do not normally produce STEAP-1 protein, an assay for the presence of this protein as a prerequisite for treatment is practicable. This, again, mimics the pattern of Herceptin® where only those breast cancers that produce the HER2 protein are candidates for treatment with Herceptin®. This is a further reminder that not each and every cancer corresponding to the organ of origin of the cell line tested need produce this protein to make the antibodies of the invention useful.

Thus, in summary, applicants wish to address the issue of whether they have provided a specific, substantial, and credible utility for the claimed peptides to produce antibodies by demonstrating that the only normal tissue in which the protein is present is prostate, a dispensable

organ, thus permitting targeted immunotherapy that nevertheless might destroy the prostate; that the presence of malignancy in the prostate can be detected using these antibodies by immunohistochemistry; and that STEAP-1 protein is produced at detectable levels in cell lines presenting tumors of organs that do not ordinarily produce this protein. It is applicants' position that, in accordance with *In re Brana*, 34 USPQ2d 1436 (Fed. Cir. 1995), this evidence is more than sufficient.

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Respectfully submitted,

By Kate H Murashige

Kate H. Murashige
Registration No.: 29,959
MORRISON & FOERSTER LLP
3811 Valley Centre Drive, Suite 500
San Diego, California 92130
(858) 720-5112

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